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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,770	07/28/2003	Arnold J. Levine	P1176R1C1	5778

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,770	LEVINE ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *1-12,18-20,22-37,39,and 41-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17,21,28 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II in the reply filed on 7/14/2006 is acknowledged.

Claims 1-43 are pending. Claims 1-12, 18-20, 22-37, 39, 41-43, drawn to non-elected inventions, are withdrawn from further consideration.

Claims 13-17, 21, 38 and 40 are examined on the merits.

Objections to the Specification

2. This application appears be a continuation of prior Application No. 09/182,562, filed 10/29/1998. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Claim Objections

3. Claims 13 and 15 are objected to for depending from claims that are withdrawn from consideration. Correction is required. For examination purposes, claims 13 and 15 are examined by considering the limitations present in claims 1 and 9.

Claim Rejections - 35 USC § 112

4. Claims 14, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is indefinite because of the recitations "human clone 65" and "mouse clone 65". The specification contains a definition that is circular (page 11, line 35 – page 12, line 1). If applicant intends a polypeptide with a specific sequence, that sequence should be identified by sequence identifier.

Claim 16 is indefinite because of the recitation "clone 65 polypeptide". The specification contains a definition that is circular (page 11, line 35 – page 12, line 1). If applicant intends a polypeptide with a specific sequence, that sequence should be identified by sequence identifier.

5. Claims 13-17, 21, 38 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this

rejection is that the specification fails to teach one of skill in the art how to use the claimed inventions.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Claims 13-17, 21, 38 and 40 are drawn to clone 65 polypeptides that comprise SEQ ID NO: 3, or are encoded by nucleic acid molecules having at least 800 nucleotides and at least about 70% sequence identity to a DNA encoding SEQ ID NO: 3, or are encoded by nucleic acid molecules comprising any of SEQ ID NOS: 11, 12, 13, 14,15, 16, 17, 18 or 19; chimeric molecules comprising clone 65 polypeptides; and to compositions comprising clone 65 polypeptides.

The specification teaches that the polypeptide comprising the amino acid sequence of SEQ ID NO: 6 is a mouse clone 65 polypeptide, whereas the polypeptide comprising the amino acid sequence of SEQ ID NO: 3 is a human clone 65 polypeptide. The mouse clone 65 polypeptide was isolated by Wnt-differential screening using suppression subtractive hybridization from a mouse mammary cell line (C57MG). The human clone 65 polypeptide was isolated from a human fetal liver cDNA library. Both the human and the mouse polypeptides have been found to be members of the Rho, Rac, and CDC42 family. The specification asserts that it is believed that these protein are involved in the up-regulation of cancer genes. However,

the specification provides no experimental evidence showing a correlation between clone 65 polypeptide expression and up-regulation of cancer genes. Furthermore, in a post-filing date publication, clone 65 polypeptides (referred to as WRCH1) are not shown to have a clear role in cancer. Kirikoshi (Kirikoshi, H. et al., International Journal of Oncology, 20: 777-783, 2002) teaches that amounts of WRCH1 mRNA is lower in some cancer lines, but either up-regulated or down-regulated in other cases of primary tumors (see abstract). Additionally, changes in mRNA levels do not necessarily correlate with changes in protein levels. For instance, McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp.2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA.

An additional post-filing date publication (Saras, J. et al. Experimental cell Research, 299: 356-369, 2004) teaches that Wrch1 is one of the least known Rho GTPases (see page 357, 1st column – 2nd column, bridging sentence). Furthermore, Saras teaches that the mechanism of action and regulation of Wrch1 is not similar to the close related Cdc42 like GTPases, and that it has unusual properties (see page 364, 2nd column). Saras also teaches that further studies will be required to gain information regarding the physiological function and regulation of Wrch1 are needed (page 368, 1st column, final paragraph). Therefore, because the specification, the prior art or the post-filing date art fails to teach a biological function of clone 65 polypeptides (referred to as Wrch-1), or a correlation with a disease, one of skill in the art would not know how to use the claimed polypeptides and compositions as of the effective filing date of this application.

The specification asserts several utilities for clone 65 polypeptides (see page 37 of the specification). One utility is an assay to determine whether TGF-β induces clone 65

polypeptides to indicate a role in cancer. However, this utility is not a substantial utility because it involves a utility that has the purpose of studying the invention itself. Other utilities that are asserted are for diagnostic, screening methods, affinity purification methods and treatment and diagnosis of cancer and a laundry list of diseases (page 38, line 22 – page 39, line 1). However, these utilities are neither substantial nor specific, because the specification fails to disclose a specific association between the expression levels or physiological functioning of clone 65 polypeptides and cancer or any of the other diseases. Thus, further experimentation would be required to determine if a use could be found for a clone 65 polypeptide in a method for diagnosis or treatment of cancer or any of the other named diseases. This further research would be directed to discovering an association between clone 65 expression levels of biological activity and cancer or any of the other name diseases, and such research would constitute research on the invention itself (See *Brenner v. Manson*, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and state, in context of the utility requirement, that " a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.")

Even if the specification taught one of skill in the art how to use a specific embodiment of a clone 65 polypeptide, for example, a polypeptide comprising the amino acid sequence of SEQ ID NO: 3, the specification fails to teach one of skill in the art how to use the variants, and mutants that are encompassed by the breadth of the claims. The claims are broadly drawn to polypeptides that are encoded by nucleic acids having at least 70% sequence identity to nucleic acids encoding SEQ ID NO: 3. It is well established that the study of the relationship between

the primary amino acid sequence and protein function is highly unpredictable. Bowie et al (Science, 247: 1306-1310, 1990) teaches that while it is known that many amino acid substitutions are possible in any given protein, the position with the protein sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Burgess et al (J. Cell Biology, 111: 2129-2138, 1990) teaches that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Lazar et al (Molecular and Cellular Biology, 8: 1247-1252, 1988) teaches that replacement of aspartic acid at position 47 with alanine or asparagines does not affect biological activity while replacement with serine or glutamic acid sharply reduces the biological activity of the protein. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Therefore, because of the unpredictability in the art, one of skill in the art would have to engage in undue experimentation to learn how to use the clone 65 variants encompassed by the claims.

Therefore, because the specification fails to provide specific correlations between expression or activity of even one embodiment of a clone 65 polypeptide and any of the diseases listed in the specification, further and undue experimentation would be required for one of skill in the art to learn how to use the claimed polypeptides for uses other than study of the claimed polypeptides. Finally, even if specification taught how to use one embodiment, this teaching would not be commensurate in scope with the scope of the claims, which encompass variants of clone 65 polypeptides.

6. Claims 13-17, 21, 38 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the specification fails to sufficiently describe the genus of polypeptides encompassed by the claims. Claims 14 and 16 are included in this rejection because it is not clear if these claims are drawn to specific sequences or to a genus of sequences.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is for purposes of the 'written description' inquiry, "*whatever is now claimed*" (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See Vas-Cath at page 1116.)

The claims are broadly drawn to polypeptides that are encoded by nucleic acid molecules having at least 70% identity to a nucleic acid molecule that encodes SEQ ID NO: 3, or that are encoded by any of the following nucleic acid sequences: SEQ ID NOS: 11, 12, 13, 14, 15,16, 17, 18 and 19, which are variants of a nucleic acid molecule that encodes SEQ ID NO: 3. Thus, the claims are broadly drawn to a genus of molecules for which the disclosure of the polypeptide sequence of SEQ ID NO: 3 and nucleic acid sequences of SEQ ID NOS: 11, 12, 13, 14, 15,16, 17, 18 and 19 are not representative. For example, the specification teaches that the mouse and human sequences are 93% homologous. Therefore, the variation between the sequences

disclosed does not appear to be as great as what is claimed (the encoding nucleic acids have only at least 70% sequence identity). For a claim drawn to a genus, the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (see Official Gazette 1241 OG 174, January 30, 2001). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112, is severable from its enablement provision. (See page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 13, 14, 16, 21 and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Hillman (US 5,840,569; issued Nov. 24, 1998; effective filing date Dec. 12, 1996; cited in the IDS).

Hillman teaches a polypeptide that has an amino acid sequence that has greater than 97% sequence identity with SEQ ID NO: 3 (an example of a clone 65 polypeptide) from amino acid 63 to 242 of SEQ ID NO: 3. Hillman teaches therapeutic compositions comprising this polypeptide (col. 21, line 61- column 22, line 6). Hillman teaches fusion proteins with a heterologous protein (see col. 17, lines 4-31). Therefore, Hillman teaches polypeptides and compositions that are the same as that claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
September 28, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER